ISSN 1948-9366 (online)

World Journal of *Gastrointestinal Surgery*

World J Gastrointest Surg 2023 September 27; 15(9): 1841-2097

Published by Baishideng Publishing Group Inc

World Journal of Gastrointestinal Surgery

Contents

Monthly Volume 15 Number 9 September 27, 2023

REVIEW

MINIREVIEWS

ORIGINAL ARTICLE

Retrospective Cohort Study

Retrospective Study

World Journal of Gastrointestinal Surgery

Monthly Volume 15 Number 9 September 27, 2023

Contents

World Journal of Gastrointestinal Surgery

Monthly Volume 15 Number 9 September 27, 2023

Contents

CASE REPORT

World Journal of Gastrointestinal Surgery

Monthly Volume 15 Number 9 September 27, 2023

Contents

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The *WJGS* is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports/Science Edition, PubMed, PubMed Central, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2023 Edition of Journal Citation Reports® cites the 2022 impact factor (IF) for *WJGS* as 2.0; IF without journal self cites: 1.9; 5-year IF: 2.2; Journal Citation Indicator: 0.52; Ranking: 113 among 212 journals in surgery; Quartile category: Q3; Ranking: 81 among 93 journals in gastroenterology and hepatology; and Quartile category: Q4.

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NAME OF JOURNAL
World Journal of Gastrointestinal Surgery

ISSN
ISSN 1948-9366 (online)

LAUNCH DATE
November 30, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Peter Schemmer

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/1948-9366/editorialboard.htm

PUBLICATION DATE
September 27, 2023

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World J Gastrointest Surg 2023 September 27; 15(9): 1969-1977

DOI: 10.4240/wjgs.v15.i9.1969

ISSN 1948-9366 (online)

ORIGINAL ARTICLE

Retrospective Study

Short- and long-term results of open *vs* laparoscopic multisegmental resection and anastomosis for synchronous colorectal cancer located in separate segments

Ji-Chuan Quan, Xin-Jun Zhou, Shi-Wen Mei, Jun-Guang Liu, Wen-Long Qiu, Jin-Zhu Zhang, Bo Li, Yue-Gang Li, Xi-Shan Wang, Hu Chang, Jian-Qiang Tang

Specialty type: Oncology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C
Grade D (Fair): D, D
Grade E (Poor): 0

P-Reviewer: Diez-Alonso M, Spain; Gad EH, Egypt

Received: May 3, 2023
Peer-review started: May 3, 2023
First decision: June 13, 2023
Revised: June 29, 2023
Accepted: July 27, 2023
Article in press: July 27, 2023
Published online: September 27, 2023

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Abstract

BACKGROUND

It remains unclear whether laparoscopic multisegmental resection and anastomosis (LMRA) is safe and advantageous over traditional open multisegmental resection and anastomosis (OMRA) for treating synchronous colorectal cancer (SCRC) located in separate segments.

AIM

To compare the short-term efficacy and long-term prognosis of OMRA as well as LMRA for SCRC located in separate segments.

METHODS

Patients with SCRC who underwent surgery between January 2010 and December 2021 at the Cancer Hospital, Chinese Academy of Medical Sciences and the Peking University First Hospital were retrospectively recruited. In accordance with the

inclusion and exclusion criteria, 109 patients who received right hemicolectomy together with anterior resection of the rectum or right hemicolectomy and sigmoid colectomy were finally included in the study. Patients were divided into the LMRA and OMRA groups (n = 68 and 41, respectively) according to the surgical method used. The groups were compared regarding the surgical procedure's short-term efficacy and its effect on long-term patient survival.

RESULTS

LMRA patients showed markedly less intraoperative blood loss than OMRA patients (100 *vs* 200 mL, P = 0.006). Compared to OMRA patients, LMRA patients exhibited markedly shorter postoperative first exhaust time (2 *vs* 3 d, P = 0.001), postoperative first fluid intake time (3 *vs* 4 d, P = 0.012), and postoperative hospital stay (9 *vs* 12 d, P = 0.002). The incidence of total postoperative complications (Clavien-Dindo grade: ≥ II) was 2.9% and 17.1% (P = 0.025) in the LMRA and OMRA groups, respectively, while the incidence of anastomotic leakage was 2.9% and 7.3% (P = 0.558) in the LMRA and OMRA groups, respectively. Furthermore, the LMRA group had a higher mean number of lymph nodes dissected than the OMRA group (45.2 *vs* 37.3, P = 0.020). The 5-year overall survival (OS) and disease-free survival (DFS) rates in OMRA patients were 82.9% and 78.3%, respectively, while these rates in LMRA patients were 78.2% and 72.8%, respectively. Multivariate prognostic analysis revealed that N stage [OS: HR hazard ratio (HR) = 10.161, P = 0.026; DFS: HR = 13.017, P = 0.013], but not the surgical method (LMRA/OMRA) (OS: HR = 0.834, P = 0.749; DFS: HR = 0.812, P = 0.712), was the independent influencing factor in the OS and DFS of patients with SCRC.

CONCLUSION

LMRA is safe and feasible for patients with SCRC located in separate segments. Compared to OMRA, the LMRA approach has more advantages related to short-term efficacy.

Key Words: Synchronous colorectal cancer; Separate segments; Laparoscopic surgery; Multisegmental resection; Short-term efficacy; Prognosis

Core Tip: The efficacy and safety of laparoscopic multisegmental resection and anastomosis (LMRA) in patients with synchronous colorectal cancer involving separate segments has not been fully evaluated. We compared the short-term efficacy and long-term prognosis between LMRA and open multisegmental resection and anastomosis, and found that the LMRA approach has more advantages related to faster postoperative recovery, less intraoperative blood loss, reduced postoperative hospital stay, fewer postoperative complications, and a greater total number of lymph nodes dissected.

Citation: Quan JC, Zhou XJ, Mei SW, Liu JG, Qiu WL, Zhang JZ, Li B, Li YG, Wang XS, Chang H, Tang JQ. Short- and long-term results of open *vs* laparoscopic multisegmental resection and anastomosis for synchronous colorectal cancer located in separate segments. *World J Gastrointest Surg* 2023; 15(9): 1969-1977
URL: https://www.wjgnet.com/1948-9366/full/v15/i9/1969.htm
DOI: https://dx.doi.org/10.4240/wjgs.v15.i9.1969

INTRODUCTION

Synchronous colorectal cancer (SCRC), a colorectal malignancy, refers to the simultaneous presence of multiple primary colorectal cancers (CRCs) in one patient. SCRC lesions can be located in the same segments, adjacent segments, or different segments of the colorectum. For patients with SCRC localized in separate segments, multisegmental resection and anastomosis are often selected for treatment. Compared to conventional surgery, multisegmental resection is less common and more difficult. Selection of the optimal surgical method to promote rapid recovery in patients with SCRC involving separate segments still requires further study.

Previous studies have shown the safety and advantages of laparoscopic surgery in treating solitary CRC[1-5]. However, to date, there are few comparisons of the application of laparoscopic multisegmental resection and anastomosis (LMRA) and open multisegmental resection and anastomosis (OMRA) for SCRC. Therefore, the safety and efficacy of LMRA are not adequately understood and require further evaluation.

To determine the efficacy and safety of LMRA in patients with SCRC involving separate segments, a retrospective two-institution investigation was performed to compare the short-term surgical results, 5-year overall survival (OS) rate, as well as the 5-year disease-free survival (DFS) rate of patients receiving LMRA and OMRA.

MATERIALS AND METHODS

Selection of patients

Patients with SCRC who underwent surgery between January 2010 and December 2021 at the Cancer Hospital, Chinese Academy of Medical Sciences and the Peking University First Hospital were included. Multiple CRC lesions were diagnosed following published guidelines[6].

The following types of patients were included: (1) SCRC patients with pathological confirmation of lesions as primary adenocarcinoma; (2) SCRC patients with one lesion in the right hemicolon and the others located in the sigmoid colon or rectum; and (3) patients receiving right hemicolectomy as well as anterior resection of the rectum or right hemicolectomy and sigmoid colectomy. The following categories of patients were excluded: (1) Those with familial adenomatous polyposis, ulcerative colitis, hereditary nonpolyposis CRC, or Lynch syndrome; (2) patients with SCRC involving the same segment; (3) patients with SCRC involving adjacent segments; (4) those receiving Hartmann's procedure or abdominal perineal resection; (5) those receiving subtotal colectomy, total colectomy, or proctocolectomy with ileoanal anastomosis; and (6) SCRC patients with distant metastasis. The selected patients were included in the LMRA and OMRA groups based on the surgical method. The study was approved by the Ethics Committee of Cancer Hospital, Chinese Academy of Medical Sciences.

Data collection

The following clinicopathological data were collected: Age, gender, abdominal surgery history, concomitant diseases, preoperative chemotherapy, carbohydrate antigen 19-9 (CA19-9) level, carcinoembryonic antigen (CEA) level, American Society of Anesthesiologists (ASA) physical status level, surgical approach (laparoscopic or open), operative time, volume of blood loss (mL), postoperative first exhaust time (d), time to first liquid diet (d), postoperative hospital stay (d), postoperative complications, classification of complications, tumor size (cm), tumor differentiation status, N stage, T stage and TNM stage, total number of positive lymph nodes (LNs), and number of LNs dissected. Pathological staging was evaluated using the American Joint Committee on Cancer (8th ed.) staging system. The Clavien-Dindo (CD) system[7] was employed to grade postoperative complications.

Follow-up

Patients were followed up through telephone calls or outpatient examination. The following time frame was chosen: every 3 mo in the first 2 years following surgery, every 6 mo at 3–5 years following surgery, and then yearly 5 years after surgery. Follow-up assessment included physical examination, determination of serum tumor marker levels, CT scans of the abdomen, chest, and pelvic area, and colonoscopy.

Statistical analysis

The Mann-Whitney *U* test or Student's *t*-test was used to compare continuous variables; Fisher's exact test or the chi-square test was used to compare categorical variables. The Kaplan-Meier analysis was employed to create survival curves. Survival differences were compared between the groups by the log-rank test. The Cox proportional hazards model was used to conduct univariate and multivariate prognostic analyses. A value of $P < 0.05$ was considered statistically significant. Statistical Product and Service Solutions (SPSS) version 26.0 from IBM (Armonk, NY, United States) was used for statistical determinations.

RESULTS

Clinicopathological characteristics

From January 2010 to December 2021, 605 SCRC patients underwent surgical treatment at the above-mentioned institutions. Of these 605 patients, 496 patients were excluded according to the aforementioned criteria. Finally, 109 patients with SCRC located in separate segments were included, with 41 and 68 patients placed in the OMRA and LMRA groups, respectively.

Clinicopathological characteristics of the patients are shown in Table 1. As noted in this table, the groups did not differ significantly in age, gender, abdominal surgery history, concomitant diseases, preoperative chemotherapy, CA19-9 and CEA levels, ASA class, postoperative chemotherapy, tumor size, tumor differentiation status, N stage, T stage, and TNM stage.

Surgical results

Table 2 presents the surgical outcomes of both groups. LMRA patients showed markedly less intraoperative blood loss than OMRA patients (100 *vs* 200 mL, $P = 0.006$). The LMRA group showed a significantly shorter postoperative first exhaust time (2 *vs* 3 d, $P = 0.001$), postoperative first fluid intake time (3 *vs* 4 d, $P = 0.012$), and postoperative hospital stay (9 *vs* 12 d, $P = 0.002$) than the OMRA group. The incidence of total postoperative complications (CD grade ≥ II) was 2.9% in the LMRA group; this percentage was markedly lower than the value (17.1%) recorded for the OMRA group ($P = 0.025$). Furthermore, LMRA patients had a lower incidence of anastomotic leakage than OMRA patients; however, the difference was nonsignificant (2.9% *vs* 7.3%, $P = 0.558$). The mean number of LNs dissected was significantly greater in LMRA patients as compared to OMRA patients (45.2 *vs* 37.3, $P = 0.020$). However, there were no significant differences in operating time, mortality rate, and number of positive LNs between the two groups.

Table 1 Basic characteristics between laparoscopic group and open group, *n* (%)

Variable	OMRA group, *n* = 41	LMRA group, *n* = 68	*P* value
Age (yr)			
≤ 65	24 (58.5)	31 (45.6)	0.190
> 65	17 (41.5)	37 (54.4)	
Gender			
Female	14 (34.1)	26 (38.2)	0.668
Male	27 (65.9)	42 (61.8)	
ASA physical status			0.058
I-II	33 (80.5)	63 (92.6)	
III	8 (19.5)	5 (7.4)	
Concomitant diseases			
No	19 (46.3)	29 (42.6)	0.707
Yes	22 (53.7)	39 (57.4)	
History of abdominal surgery			
No	30 (73.2)	56 (82.4)	0.255
Yes	11 (26.8)	12 (17.6)	
Preoperative chemotherapy			
No	39 (95.1)	68 (100)	0.139
Yes	2 (4.9)	0 (0)	
Tumor size[1], cm			
≤ 5	20 (50.0)	40 (58.8)	0.373
> 5	20 (50.0)	28 (41.2)	
Tumor differentiation			
Well-moderate	24 (58.5)	32 (47.1)	0.245
Poor	17 (41.5)	36 (52.9)	
pT stage			
T1-T2	2 (4.9)	7 (10.3)	0.525
T3-T4	39 (95.1)	61 (89.7)	
pN stage			
N0	16 (39.0)	25 (36.8)	0.915
N1	19 (46.3)	31 (45.6)	
N2	6 (14.6)	12 (17.6)	
Stage			
I	1 (2.4)	6 (8.8)	0.338
II	15 (36.6)	19 (27.9)	
III	25 (61.0)	43 (63.2)	
CEA			
≤ 5	19 (46.3)	31 (45.6)	0.929
> 5	13 (31.7)	20 (29.4)	
Unknown	9 (22.0)	17 (25.0)	
CA199			
≤ 37	28 (68.3)	42 (61.8)	0.696

> 37	3 (7.3)	9 (13.2)	
Unknown	10 (24.4)	17 (25.0)	
Postoperative chemotherapy			
No	20 (48.8)	30 (44.1)	0.636
Yes	21 (51.2)	38 (55.9)	

[1]Unknown for one patient.
OMRA: Open multisegmental resection and anastomosis; LMRA: Laparoscopic multisegmental resection and anastomosis; CA19-9: Carbohydrate antigen 19-9; CEA: Carcinoembryonic antigen; ASA: American Society of Anesthesiologists.

Table 2 Surgical results between laparoscopic group and open group

Variable	OMRA group, *n* = 41	LMRA group, *n* = 68	*P* value
Operative time (min)	253.0 ± 101.9	274.0 ± 83.4	0.244
Blood loss (mL)	200 (30-600)	100 (20-600)	0.006
Time to first exhaust (d)	3 (1-6)	2 (1-4)	0.001
Time to first liquid diets (d)	4 (2-9)	3 (2-6)	0.012
Postoperative complications (Grade II-V)	7 (17.1)	2 (2.9)	0.025
Ileus	2 (4.9)	0 (0.0)	0.139
Anastomotic leakage	3 (7.3)	2 (2.9)	0.558
Cerebral infarction	1 (2.4)	0 (0.0)	0.376
Abdominal incision infection	1 (2.4)	0 (0.0)	0.376
No. of retrieved lymph nodes	37.3 ± 17.1	45.2 ± 16.8	0.020
No. of positive lymph nodes	1 (0-13)	1 (0-15)	0.542
Mortality	0 (0)	0 (0)	1.000
Postoperative hospital stay, median, range, days	12 (7-34)	9 (3-30)	0.002

OMRA: Open multisegmental resection and anastomosis; LMRA: Laparoscopic multisegmental resection and anastomosis.

Long-term oncological consequences

The median follow-up period was 53.5 mo for all patients. OMRA patients had 3-year and 5-year OS rates of 87.5% and 82.9%, respectively; these rates for LMRA patients were 84% and 78.2%, respectively. Additionally, the 3-year and 5-year DFS rates for OMRA patients were 82.6% and 78.3%, respectively; these rates for LMRA patients were 79.3% and 72.8%, respectively. Both groups showed no significant differences in OS (P = 0.690) and DFS (P = 0.694) rates (Figure 1). According to the multivariate prognostic analysis, N stage was an independent prognostic factor for OS [hazard ratio (HR) = 10.161, P = 0.026] and DFS (HR = 13.017, P = 0.013) (Table 3).

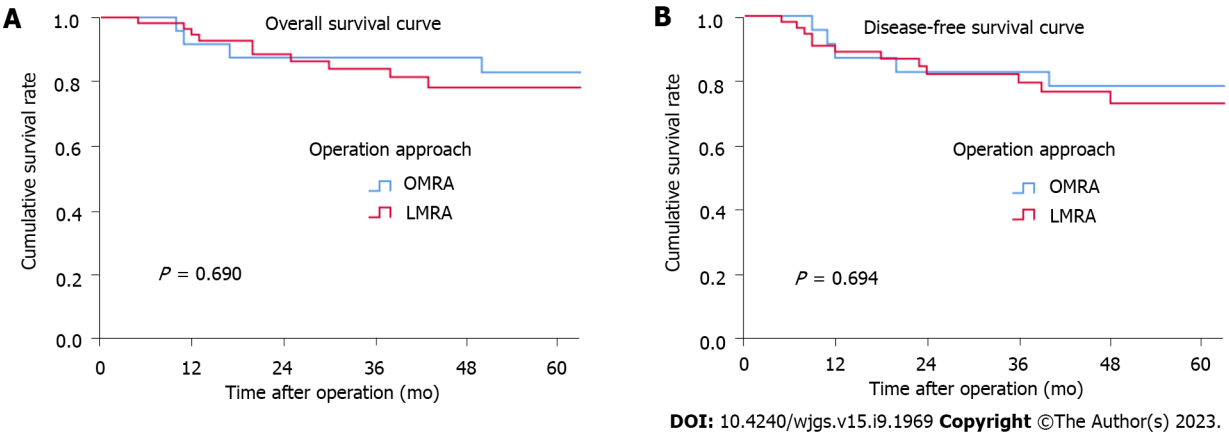
DISCUSSION

SCRC involving separate segments is a relatively rare type of CRC. Surgeons can choose two regional resections and anastomoses for preserving the left hemicolon or extensive resection, for example, total colectomy, subtotal colectomy, or proctocolectomy with ileoanal anastomosis. Which is the best treatment option is still unresolved. Lee *et al*[8] retrospectively analyzed the postoperative bowel movements in SCRC, and found that the mean number of bowel movements in a two regional resections group and an extensive resection group was 1.9 times and 4.3 times, respectively, with a significant difference between the two groups. You *et al*[9] compared the bowel function and quality of life between patients with extended resections and segmental colonic resections. The results showed that median daily stool frequency after segmental resections, ileosigmoid anastomosis and ileorectal anastomosis was 2, 4 and 5, respectively, and the overall quality of life was 98.5, 94.9, and 91.2, respectively. As multisegmental resection provides better postoperative defecation function and quality of life[8,9] and does not increase complications such as anastomotic leakage[9], this technique is recommended by some researchers.

Table 3 Univariate and multivariate analysis of overall survival and disease-free survival

Variable	Overall survival				Disease-free survival			
	Univariable analysis		Multivariate analysis		Univariable analysis		Multivariate analysis	
	HR (95%CI)	*P* value	HR (95%CI)	*P* value	HR (95%CI)	*P* value	HR (95%CI)	*P* value
Age (> 65/≤ 65 yr)	2.830 (0.983-8.150)	0.054	2.378 (0.793-7.128)	0.122	2.048 (0.779-5.384)	0.146	1.869 (0.674-5.188)	0.230
Gender (male/female)	1.051 (0.382-2.894)	0.923			1.180 (0.436-3.191)	0.744		
CEA level (> 5/≤ 5)	1.278 (0.389-4.198)	0.686			1.098 (0.348-3.465)	0.873		
CA19-9 level (> 37/≤ 37)	1.951 (0.506-7.521)	0.332			1.304 (0.285-5.958)	0.732		
ASA physical status (III/I-II)	2.565 (0.817-8.050)	0.106			2.280 (0.655-7.940)	0.195		
Tumor differentiation (poor/well- moderate)	0.918 (0.340-2.478)	0.866			1.119 (0.431-2.906)	0.817		
Tumor size (> 5/≤ 5 cm)	1.058 (0.383-2.920)	0.913			0.863 (0.328-2.269)	0.764		
T stage (T3-T4/T1-T2)	0.994 (0.130-7.627)	0.994			1.302 (0.172-9.854)	0.798		
N stage (N1-N2/N0)	11.266 (1.487-85.384)	0.019	10.161 (1.327-77.790)	0.026	13.414 (1.775-101.359)	0.012	13.107 (1.719-99.925)	0.013
Operative approach (LMRA/OMRA)	1.240 (0.426-3.611)	0.693	0.834 (0.274-2.534)	0.749	1.233 (0.432-3.516)	0.695	0.812 (0.269-2.454)	0.712

OMRA: Open multisegmental resection and anastomosis; LMRA: Laparoscopic multisegmental resection and anastomosis; CA19-9: Carbohydrate antigen 19-9; CEA: Carcinoembryonic antigen; ASA: American Society of Anesthesiologists; HR: Hazard ratio; CI: Confidence interval.



DOI: 10.4240/wjgs.v15.i9.1969

Figure 1 Kaplan-Meier survival analysis. A: Overall survival curves for patients with different operative methods; B: Diseases-free survival curves for patients with different operative methods. OMRA: Open multisegmental resection and anastomosis; LMRA: Laparoscopic multisegmental resection and anastomosis.

Following advances in laparoscopic techniques, several studies have confirmed that laparoscopic radical resection of CRC is safe and reliable; moreover, it can achieve the same curative effect as open surgery[10-14] and offers the advantages of minimally invasive surgery, such as small incision, mild postoperative pain, and rapid recovery[15,16]. However, unlike conventional CRC surgery, surgical treatment of SCRC with multisegmental resection is more difficult as more anastomoses are required. Presently, there are limited reports on the differences between laparoscopic and open surgical approach for SCRC involving separate segments. These studies are limited to single-center investigations with few patients and are mainly focused on the analysis of short-term efficacy; consequently, they lack a comparison of long-term prognosis[17,18]. Here, we studied patients from two institutions with SCRC located in separate segments. These patients underwent either LMRA or OMRA as curative surgery. We found that intraoperative blood loss together with postoperative parameters such as postoperative first exhaust time, postoperative first fluid intake time, the incidence of postoperative complications, and postoperative hospital stay were less in LMRA patients when compared with those in

OMRA patients. Furthermore, LMRA patients had more LNs dissected than OMRA patients, while the prognosis for both groups was similar. To our knowledge, this study includes the largest sample size for comparing LMRA and OMRA approaches with regard to short-term efficacy as well as long-term results.

Intraoperative blood loss and the incidence of postoperative complications are critical parameters for evaluating whether a surgical procedure is safe. Previous studies have confirmed that laparoscopic surgery has more advantages than open surgery for solitary CRC in terms of less intraoperative blood loss[19-22], reduced postoperative oral intake time[21,22], and shorter postoperative hospital stay[21-25]. Moreover, previous single-center, small-sample studies have reached the same conclusion for patients with SCRC involving different segments. Takatsu *et al*[17] compared the short-term efficacy of LMRA and OMRA in 42 patients with SCRC located in different segments; the authors noted that postoperative hospital stay and intraoperative blood loss were significantly decreased in the laparoscopic group as compared to the open surgery group. Nozawa *et al*[18] performed a single-center study of 25 patients with SCRC; the authors found that the laparoscopic group showed less intraoperative blood loss than the open surgery group. Here, we analyzed the surgical results of 109 patients with SCRC located in separate segments and found significantly less intraoperative blood loss in LMRA patients than in OMRA patients. Moreover, the total postoperative complication as well as hospital stay were remarkably better in LMRA patients. Furthermore, the operating time was not significantly increased in LMRA patients.

The number of dissected LNs is another crucial factor in evaluating radical surgery of CRC. In accordance with the guidelines of the National Comprehensive Cancer Network, the number of dissected LNs should be 12 or more after radical surgery of CRC. If the number of dissected LNs is small, the final staging will be affected. For SCRC located in separate segments, the number of dissected LNs is another vital indicator in evaluating surgical quality. Laparoscopy enables magnification of the operative field; hence, the dissection of LNs by laparoscopy is more precise than that by open surgery. A significantly higher number of LNs have been dissected by laparoscopy than by traditional open surgery [17]. The present study revealed that the average number of LNs dissected in LMRA patients was significantly more than that in OMRA patients; this finding was in agreement with the result of Takatsu *et al*[17]. However, both groups did not significantly differ in the number of positive LNs.

According to several studies, both laparoscopic and open surgeries have similar oncological results[26-30]. However, for SCRC located in separate segments, comparative studies on the long-term efficacy of LMRA and OMRA are presently inadequate. In our study, the 5-year OS rates of LMRA and OMRA patients were 78.2% and 82.9%, respectively, while the 5-year DFS rates of LMRA and OMRA patients were 72.8% and 78.3%, respectively. Both groups did not markedly differ in long-term prognosis. We further performed a multivariate prognostic analysis and found that the N stage was the sole independent prognostic factor that affected DFS and OS.

There are a few limitations in this research. First, selection bias probably existed due to the study's retrospective nature. Second, some patients' clinical data were incomplete, such as the time of first ambulation and postoperative pain score; thus, we could not compare and analyze the differences between open and laparoscopic approaches with regard to these aspects. Third, as the incidence of SCRC located in separate segments is low, although the sample size in this study is the largest thus far, the number of patients included in the analysis is still small. Therefore, multicenter prospective studies are needed in the future to confirm the advantages of LMRA.

CONCLUSION

LMRA is safe and feasible for SCRC located in separate segments; moreover, it has the benefits of less bleeding, rapid recovery, shorter postoperative hospital stay, reduced complications, a greater total number of LNs dissected and achieves the same long-term oncological outcomes as OMRA.

ARTICLE HIGHLIGHTS

Research background

Limited studies have focused on the differences between laparoscopic multisegmental resection and anastomosis (LMRA) and open multisegmental resection and anastomosis (OMRA) for synchronous colorectal cancer (SCRC) involving separate segments. Therefore, more studies on the safety and efficacy of LMRA are needed.

Research motivation

To assess the efficacy and safety of LMRA in patients with SCRC involving separate segments.

Research objectives

The objectives of this study were to compare the short-term efficacy and long-term oncological consequences of OMRA as well as LMRA for SCRC located in separate segments.

Research methods

A retrospective two-institution investigation was performed in 109 patients who received right hemicolectomy together with anterior resection of the rectum or right hemicolectomy and sigmoid colectomy. The OMRA and LMRA groups

included 41 and 68 patients, respectively. The clinicopathological characteristics and surgical results were compared between the groups, and the Cox proportional hazards model was used to conduct univariate and multivariate prognostic analyses.

Research results

LMRA patients showed significantly shorter postoperative first exhaust time, postoperative first fluid intake time, and postoperative hospital stay than OMRA patients. Intraoperative blood loss, and the incidence of total postoperative complications (Clavien-Dindo grade: ≥ II) were markedly less in the LMRA group. The mean number of lymph nodes dissected was significantly higher in the LMRA group. Prognostic analysis showed that N stage was the independent prognostic factor for overall survival and disease-free survival.

Research conclusions

On the basis of this study, we conclude that LMRA has some short-term advantages compared with OMRA, and is safe and feasible for patients with SCRC located in separate segments.

Research perspectives

Future multicenter prospective studies are needed to further confirm the advantages of LMRA.

FOOTNOTES

Author contributions: Quan JC and Zhou XJ contributed equally to this work; Quan JC and Chang H wrote the manuscript; Tang JQ, Zhou XJ and Wang XS conceived and designed the study; Quan JC, Liu JG, Chang H, Mei SW and Zhou XJ collected the data; Zhang JZ, Qiu WL, Li B and Li YG analyzed the data; all authors made critical revisions for the manuscript and approved the final manuscript.

Institutional review board statement: This study was approved by the Ethics Committee of Cancer Hospital, Chinese Academy of Medical Sciences.

Informed consent statement: Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

Conflict-of-interest statement: The authors declare no conflict of interest.

Data sharing statement: No additional data are available.

Country/Territory of origin: China

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S-Editor: Yan JP
L-Editor: A
P-Editor: Yan JP

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